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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/415,540 | 10/08/1999 | PHILLIP R. HAWKINS | PF-0148-3 CPA | 4965 |

27904 7590 07/25/2003

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| EXAMINER | |
|---|---|
| SLOBODYANSKY, ELIZABETH | |
| ART UNIT | PAPER NUMBER |
| 1652 | |

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/415,540 | HAWKINS ET AL. | |
| | Examiner | Art Unit | |
| | Elizabeth Slobodyansky | 1652 | |

*-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**P riod for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

In view of the Appeal Brief filed on May 9, 2003, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

The AF amendment filed April 7, 2003 amending claim 20 has been entered. Claims 18-20 are pending.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 19, with dependent claims 18 and 20, is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in

such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 19 recites "a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1", thus encompassing all allelic variants of SEQ ID NO:1. There is no limitation on the function of the encoded protein. Thus, the genus of polynucleotides of claim 19 encodes proteins having pyrophosphatase activity and many variants thereof with unknown functions.

Allelic variants are alternate forms of a gene which have at least one mutation in the nucleotide sequence which may result in mRNAs (polypeptides) with altered function. With regard to a naturally-occurring human polynucleotide sequence variant, there is no description of any mutational site that exist in nature, and there is no description of how the structure of SEQ ID NO:2 relates to the structure of any allele including strictly neutral alleles. The general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others. Thus the claimed genus is highly variable with the potential to encode proteins with widely variant functions. The common attributes of the genus are not

described. Therefore, one of skill in the art would not conclude that applicant was in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the naturally-occurring genus and is insufficient to support the claims.

Claims 18 and 20 depend from claim 19 and are drawn to a method of use of a diverse genus of a probe comprising at least 60 contiguous nucleotides of a sequence completely complementary to SEQ ID NO: 2 that specifically hybridizes to a polynucleotide of claim 19. The genus of said probes includes many structurally and functionally different species.

The specification discloses only a single species of the claimed genus, a probe consisting of a fragment of SEQ ID NO:2 consisting of at least 60 contiguous nucleotides of sequence of SEQ ID NO: 2. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties common to the entire genus of said nucleic acids and fails to provide any structure: function correlation present in all members of the claimed genus.

Therefore, based on the instant disclosure, in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of a polynucleotide probe comprising at least 60 nucleotides that are completely complementary to SEQ ID NO:2. Therefore, a naturally-occurring human DNA encoding a polypeptide comprising a sequence having

90% identity to SEQ ID NO:1 and having an undisclosed function and a method of use of a polynucleotide probe comprising at least 60 contiguous nucleotides that are completely complementary to SEQ ID NO:2 lack sufficient written description needed to practice the invention of claims 18-20.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al. (A) or Hillier et al. (B).

Hillier et al. (A), (GenBank accession H50229, September 19, 1995) teach a human EST of 520 bp that comprises more than 200 contiguous nucleotides of SEQ ID NO:2. They teach that said EST is homologous to bovine inorganic pyrophosphatase.

Hillier et al. (B), (GenBank accession W67406, June 14, 1996) teach a human EST of 437 bp that comprises 436 contiguous nucleotides of SEQ ID NO:2. They teach that said EST is homologous to bovine inorganic pyrophosphatase.

Each of these EST sequences comprises at least 60 contiguous nucleotides of SEQ ID NO:2.

Therefore, as knowledge of all the genes encoded by the human genome is important for understanding and/diagnosing human diseases or genetically determined drug interactions and for understanding many other human cellular processes, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use these cDNA fragments as hybridization probes for detecting a full-length target polynucleotide that specifically hybridizes thereto. Given the presence in a sample of SEQ ID NO:2 or a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1", it will specifically hybridize with each of the ESTs taught by Hillier et al. (A) and Hillier et al. (B).

It would have been further obvious to one of ordinary skill in the art at the time the invention was made to amplify the target polynucleotide by PCR before hybridization as it is routinely performed in the art.

***Response to Arguments***

Applicant's arguments filed May 9, 2003 have been fully considered but they are not persuasive.

With regard to the wriiten description rejection, Applicants argue that "Mention of representative compounds encompassed by generic claim language ***clearly is not required by section 112 or any other provision of the stature*** .." (Brief on Appeal,

page 4, last paragraph). Applicants cite that "***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other language***" and further "An applicants may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., *complete or partial structure*, ..."(page 5). Applicants conclude that **"The specification provides an adequate written description of the claimed "variants" of SEQ ID NO:1"** (page 5). Applicants continue to state that SEQ ID NO:1 and SEQ ID NO:2 are described as are "polynucleotide sequence variants which encode 90% homologs of SEQ ID NO:1" (page 6, second paragraph). Applicants continue "the specification also describes ... how to use BLAST to determine whether a given sequence falls within the "at least 90% polypeptide sequence identity" scope" (page 6, second paragraph). Applicants stress that "The present application also describes how to identify, or make, the claimed polynucleotides" (page 6, 3rd paragraph). Applicants argue that claim 19 is drawn to "***a naturally-occurring polynucleotide sequence variant***" (page 6, last paragraph). These arguments are disagreed with because the issue of "determination of how to identify, or make" is an enablement matter and is different from the written description. In this case there is no need to make the variants, they have been made by Nature.

Applicants further argue that the claimed naturally-occurring polynucleotide sequence actually exists. They state that "Applicants provided 3 examples of human

polynucleotides that are at least 90% identical to SEQ ID NO:1. Applicants have also found a sequence (g4583153) which is 99% and thus a variant of SEQ ID NO:1 (Exhibit A)" (page 7). This is not persuasive because while (g4583153, April 14, 1999) is a variant (described by others after the filing date), said variant was not described in and is unpredictable from the specification.

Applicants further argue that the current claims are fundamentally different from the types of claims the court has found to lack sufficient written description as the current claims recite the genus of polypeptides claimed in strictly structural terms while the claims found to lack written description in cases such as *Fiers v. Revel* (25 USPQ2d 1601) and *University of California v. Eli Lilly and Co.* (43 USPQ2d 1398) define the claimed genus in strictly functional terms (pages 8-13). While it acknowledged that the current claims differ from those held by the court to lack sufficient written description, as discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the

species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of Claims 18-20 includes species which are widely variant in function, i.e., allelic variants of SEQ ID NO:2 and all other loci which encode proteins having 90% identity to SEQ ID NO:1. Allelic variants encode polypeptides **whose function may or may not be altered**. Claims 18 and 20 are drawn to a method of use of a diverse genus of a probe comprising at least 60 nucleotides complementary to SEQ ID NO: 2. This genus includes many structurally and functionally unrelated DNAs. It encompasses polynucleotides encoding polypeptides with pyrophosphatase activity, those which lack such activity but are capable of hybridizing at unspecified conditions to a polynucleotide of claim 19 as well as an enormous number of polynucleotides encoding polypeptides with neither of these functions, but possibly other undisclosed functions. As such, neither the description of the structure and function of SEQ ID NO:1 nor the disclosure solely structural features

present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Applicant should note that the claims of the '740 patent in the *Lilly* case are limited by **both** structural limitations (the recited generic formula) and functional limitations (coding for human preproinsulin) and thus puts the artisan in possession of the attributes and features of all members of the claimed genus.

Applicants further argue that "In accordance with Brenner et al, naturally occurring molecules may exist which could be characterized as human pyrophosphatase proteins and which have as little as 40% identity over at least 70 residues to SEQ ID NO:1" (page 10). This is not persuasive because while said molecules definitely may exist, they are not described in and are unpredictable from the specification. *One skilled in the art can not visualize these naturally occurring sequences after reading the specification.* Furthermore, Brenner et al. dealt with known sequences for which the function was established. They compared structural relationship among proteins for which the function was previously empirically established. In the instant case, the function of allelic variants is not described. It can be pyrophosphatase or other undisclosed functions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

July 23, 2003

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